Remarks

This is submitted in response to the non-final Office Action mailed March 16, 2007. Claims 1-13, and 15-18 were examined. Claims 19-31 were withdrawn by the Office following restriction, and are now canceled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of the canceled claims in one or more continuing applications.

In this paper, claim 1 is amended to incorporate dependent claim 4, which is canceled. Claims 2-3, 6-13, and 15 are editorially changed without prejudice for correct dependent reference according to customary U.S. practice. Claim 16 is amended to include the date of deposit and the specification is amended to include the depository information and date of deposit. Claim 17 is canceled without prejudice or disclaimer. Claim 18 is currently amended into independent form. Claims 32-39 are added. Support for the amendments and new claims is found throughout the specification, including for instance, Example 2 at pages 24-28, and original claims 2-10 and 16.

Claim Objections

2. The rejection of claims 2-13, 15 and 18 for informalities in referral of the dependent claims to the independent claims has been obviated by amendment. Removal of the objection is requested.

Claim Rejection – 35 U.S.C. §112 --Enablement

3. The rejection of claim 16 for failing to comply with the deposit requirements has been obviated by submission of a STATEMENT and DECLARATION attesting that the deposit was made under the provisions of the Budapest Treaty and assures public availability. A copy of the deposit certificate and statement of viability from the DSMZ will follow shortly. Removal of the rejection is requested following submission of the deposit documents.

Claim Rejection – 35 U.S.C. § 102(b)

4. Claims 1-3, 5, 17 and 18 stand rejected for anticipation in view of Stingl (1998) *Differentiation* 63:201-13. This rejection is traversed.

Applicants do not concede that Stingl anticipates the cells described in claims 1-3, and 5. To facilitate further prosecution, claim 1 has been amended to incorporate the subject matter of claim 4. Claim 1, as amended, is directed to an immortalized cell, which is not taught by Stingl. Hence, claims 1-3 and 5 are not anticipated by Stingl. Withdrawal of the rejection is requested.

Rejection of claim 17 is rendered moot by cancellation of claim 17 without prejudice or disclaimer.

Claim 18, as amended into independent form, specifies method steps of passing the cells from primary culture through an anti-sialomucin column followed by retention of the flow-through in an anti-ESA column. These steps are not taught by Stingl. For at least those reasons, claim 18 is not anticipated by Stingl. Withdrawal of the rejection is requested.

Claim Rejection – 35 U.S.C. § 103

5. Claims 1, 4, 6-13, and 15 stand rejected as allegedly obvious in view of Stingl (1998) *Differentiation* 63:201-13, taken with Wazer (1995) *PNAS* 92:3687-91. This rejection is traversed.

Independent claim 1, as amended, is directed to an **immortalized** cell which is capable of forming a cell culture comprising cells which are positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-), so-called (ESA+/MUC-) cells.

To make a prima facie case of obviousness, all the limitations of the claims must be taught or suggested in the references cited by the Examiner and all the teachings of the prior art need to suggest the claimed subject matter to the person of ordinary skill in the art. *In re Kotzab*, 217 F.3d 1365, 1370 (Fed. Cir. 2000). Applicants submit that the Examiner has failed to make the required prima facie case, as the cited references, either alone or in combination, do not teach or suggest the claimed immortal cells and the references as combined are unlikely to succeed.

Stingl et al. acquire their *possibly* bipotent progenitors of the MUC-negative and ESA-positive kind by a FACS (fluorescence-activated cell sorting and cloning procedure) comprising anti-CALLA and anti-ESA described on page 203 of *Differentiation*. There is a problem with Stingl's cells. Stingl's cells lack the capability to be successfully immortalised. In the nearly 10

years since Stingl's initial isolation method, this group has not been able to generate an immortalised cell having the asserted phenotype. The inventors of the present application also attempted to immortalize cell's acquired according to Stingl's teachings and were unsuccessful.

Stingl demonstrates **only** primary cell culture of the cells asserted to have MUC-negative and ESA-positive kind phenotype. Wazer demonstrates immortalization of mixed cell types derived from mammary tissue and consequently would not recognize failure or problems with immortalization of a particular cell type. Consequently, the general teaching of Wazer regarding methods of forming immortalized cells is not sufficient to correct the lack of capability inherently present in Stingl's cells. Hence, even if Wazer's teachings are applied to Stingl's cells, there is not a likelihood of success to generate an immortalized cell of the specified phenotype.

In contrast to Stingl and Wazer, the present inventors used a different approach. The approach described in the present application is based on pursuing the flow-through from an immunomagnetic separation of luminal cells through two consecutive anti-sialomucin columns. See, description at page 26, line 35. It was in fact surprising that the present inventors discovered that the subrabasal-derived epithelial cells obtained by combining this flow-through with a further retention in an anti-ESA column actually generated an enriched MUC-negative/ESA-positive cell population, which were suitable for establishment of an immortalized cell line. Consequently, the cells and immortalized cells of the present disclosure are different from those of the art as demonstrated by at least the suitability of the cells for immortalization.

For at least the above reasons, the combination of Stingl and Wazer fail render obvious the claimed immortalized cell(s) of claims 1, 4, 6-13, and 15. Withdrawal of the rejection is respectfully requested.

In conclusion, the method for enrichment of a cell population and the cells acquired by that method which are capable of being immortalized, and demonstrate proliferation and differentiation into cells of mammary gland luminal epithelial and myoepithelial cell lineages, as well as, positive staining for the luminal epithelial marker ESA (ESA+) and negative staining for sialomucin (MUC-) are novel and non-obvious over the cited art. In particular, a specific example of such cells has been deposited under the Budapest Treaty at DSM ACC 2529.

Favorable reconsideration in the form of a Notice of Allowance is requested. Please contact the undersigned attorney with any questions regarding this application.

Respectfully submitted,
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